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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/060,294 04/15/98 JENSEN

M P60953US1

HM12/0709

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THE JENIFER BUILDING
400 SEVENTH STREET NW
WASHINGTON DC 20004

EXAMINER

ART UNIT	PAPER NUMBER
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1647

DATE MAILED:

07/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory ActionApplication No.
09/060,294Applicant(s)
Jensen et al.Examiner
David RomeoArt Unit
1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 Jun 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ In view of the early submission of the proposed reply (within two months as set forth in MPEP § 706.07 (f)), the period for reply expires on the mailing date of this Advisory Action, OR continues to run from the mailing date of the final rejection, whichever is later. In no event, however, will the statutory period for the reply expire later than SIX MONTHS from the mailing date of the final rejection.

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 18 Jun 2001. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will be entered upon the timely submission of a Notice of Appeal and Appeal Brief with requisite fees.
3. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search. (See NOTE below);
- (b) ☐ they raise the issue of new matter. (See NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE:

4. ☐ Applicant's reply has overcome the following rejection(s): _____
5. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claim(s).
6. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See the attachment.
7. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
8. ☒ For purposes of Appeal, the status of the claim(s) is as follows (see attached written explanation, if any):
Claim(s) allowed: none
Claim(s) objected to: none
Claim(s) rejected: 50-76
9. ☐ The proposed drawing correction filed on _____ a) ☐ has b) ☐ has not been approved by the Examiner.
10. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
11. ☐ Other: _____

David Romeo
DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

Art Unit: 1647

Attachment to Paper No. 21 (Advisory Action)

1. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention that, although one could immunize against TNF- α , unless the antibodies produced were neutralizing antibodies then vaccinating against TNF- α would serve no purpose, because the prior art recognizes that neutralizing antibodies represent a small subset of the total antibody titer and it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention that only neutralizing antibodies would block TNF- α activity. The prior art recognizes that there are neutralizing and non-neutralizing TNF- α antibodies and one of ordinary skill in the art would be motivated to select for neutralizing antibodies because the generation of neutralizing antibodies would provide an efficacious vaccine, whereas non-neutralizing antibodies would not. Furthermore, the prior art recognizes that an antibody binding TNF- α sufficiently close to a putative TNF- α receptor binding site blocks the receptor binding.

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Furthermore, Panina-Bordigon at page 2237, left column, teaches that the immunogenicity of a given epitope is dependent upon the generation of the appropriate fragment, the presence of an MHC molecule that binds this fragment and the presence of T cells capable of recognizing the complexes. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to insert the T cell epitope adjacent to a TNF- α epitope, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because the immunogenicity of a given epitope is dependent upon the generation of the appropriate fragment, the presence of a T cell epitope would permit a given epitope to bind an MHC molecule via the T cell epitope, thereby allowing recognition by T cells capable of recognizing the complexes.

The prior art provides the requisite motivation to select between working analogs and non-working analogs and guides one of ordinary skill in the art to select for the proper sites for substitution. In view of the combined teachings of the prior art the teachings of the instant application cannot be considered as surprising and unexpected. With respect to the present specification at page 18, lines 17-32, although immunogenicity is required for vaccination, immunogenicity, in the absence of neutralization, is not sufficient for vaccination because non-neutralizing antibodies would not block TNF- α biological activity and it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to select for those immunization reagents and procedures that produce neutralizing antibodies.

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2. Applicants are reminded that:

- a. The amendment filed 7/20/00 (Paper No. 13) has been entered in part. The amendment to the Abstract has not been entered because a new abstract on a separate sheet is required. The amendments to the specification at page 50, lines 27 and 28, have not been entered because the indicated insertion points do not occur at the indicated positions
- b. The abstract of the disclosure is objected to because it is not a single paragraph. Correction is required.
- c. The application is not fully in compliance the sequence rules, 37 C.F.R. § 1.821-1.825. Correction is required.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.


DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

JULY 3, 2001